

## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
6 November 2003 (06.11.2003)

PCT

(10) International Publication Number  
**WO 2003/091264 A3**

(51) International Patent Classification<sup>7</sup>: **C07F 9/38**, 9/40, A61K 31/4155

(21) International Application Number: **PCT/US2003/012926**

(22) International Filing Date: 25 April 2003 (25.04.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/375,665	26 April 2002 (26.04.2002)	US
60/375,834	26 April 2002 (26.04.2002)	US
60/375,779	26 April 2002 (26.04.2002)	US
60/375,622	26 April 2002 (26.04.2002)	US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier applications:

US	60/375,665 (CON)
Filed on	26 April 2002 (26.04.2002)
US	60/375,834 (CON)
Filed on	26 April 2002 (26.04.2002)
US	60/375,779 (CON)
Filed on	26 April 2002 (26.04.2002)
US	60/375,622 (CON)
Filed on	26 April 2002 (26.04.2002)

(71) Applicant (for all designated States except US): **GILEAD SCIENCES, INC.** [US/US]; 333 Lakeside Drive, Foster City, CA 94404 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **CHEN, James, M.** [US/US]; 4015 Marblehead Drive, San Ramon, CA 94583 (US). **CHEN, Xiaowu** [US/US]; 377 Laurie Meadows Drive, Apt. 319, San Mateo, CA 94403 (US). **KIM, Choung, U.** [US/US]; 1750 Elizabeth Street, San Carlos,

CA 94070 (US). **LEE, William, A.** [US/US]; 749 Anderson Drive, Los Altos, CA 94024 (US). **LEE, Christopher, P.** [US/US]; 65 Hermann Street, #5, San Francisco, CA 94102 (US). **TARIO, James, D.** [US/US]; 142 Elm Street, Apt. 205, San Mateo, CA 94401 (US). **XU, Lianhong** [US/US]; 640 Hobart Avenue, San Mateo, CA 94402 (US). **NELSON, Peter, H.** [US/US]; 42 San Juan Court, Los Altos, CA 94022 (US).

(74) Agents: ANDRUS, Alex et al.; Gilead Sciences, Inc., 333 Lakeside Drive, Foster City, CA 94404 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report: 11 March 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: NON NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS

(57) Abstract: Phosphorus-substituted imidazole compounds with anti-HIV properties having use as therapeutics and for other industrial purposes are disclosed. The compositions inhibit reverse transcriptase activity and are useful therapeutically for the inhibition of such enzymes, as well as in assays for the detection of such enzymes.

WO 2003/091264 A3

## INTERNATIONAL SEARCH REPORT

PCT/US 03/12926

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 7 C07F9/38 C07F9/40 A61K31/4155

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07F A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01 96329 A (SHINOGI & CO., LTD) 20 December 2001 (2001-12-20)	1-7, 20-90, 161-168
P, Y	page 24, line 13 - line 14 & EP 1 295 879 A (SHIONOGI & CO) 26 March 2003 (2003-03-26)	1-7, 20-90, 161-168
Y	the whole document --- WO 02 03997 A (GIRARDET JEAN LUC ;ICN PHARMACEUTICALS (US); PIETRZKOWSKI ZBIGNIEW) 17 January 2002 (2002-01-17)	1-7, 20-90, 112-138, 140-147, 161-168
	page 3, line 6 -page 7, line 12; claims 6,15 --- -/-	

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

## ° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

4 December 2003

Date of mailing of the international search report

23.01.2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Richter, H

## INTERNATIONAL SEARCH REPORT

PCT/US 03/12926

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6 312 662 B1 (ROBINSON EDWARD D ET AL) 6 November 2001 (2001-11-06)  column 43, line 27 -column 50, line 10; claim 1 ---	1-7, 20-90, 112-138, 140-147, 161-168
Y	US 5 413 996 A (BODOR NICHOLAS S) 9 May 1995 (1995-05-09)  the whole document ---	1-7, 20-90, 112-138, 140-147, 161-168
P, X	MENENDEZ-ARIAS L: "Targeting HIV: antiretroviral therapy and development of drug resistance" TRENDS IN PHARMACOLOGICAL SCIENCES, ELSEVIER, AMSTERDAM, NL, vol. 23, no. 8, 1 August 2002 (2002-08-01), pages 381-388, XP004386181 ISSN: 0165-6147 the whole document ---	1-7,13, 20-90, 161-168
X	VIELHABER, BERND: "Bericht vom 3rd International Workshop on Salvage Therapy for HIV-Infection, 12-14. April 2000, Chicago, Teil I" DEUTSCHE AIDS-HILFE E.V. FAXREPORT ZU HIV UND AIDS, no. 9 and 10, - 29 May 2000 (2000-05-29) pages 1-12, XP002247382 Berlin page 3, column 1, line 1 - line 23 ---	1-3, 161-168
Y	CLERCQ DE E: "NEW DEVELOPMENTS IN ANTI-HIV CHEMOTHERAPY" CURRENT MEDICINAL CHEMISTRY, BENTHAM SCIENCE PUBLISHERS BV, BE, vol. 8, no. 13, November 2001 (2001-11), pages 1543-1572, XP009012547 ISSN: 0929-8673 page 1556 -page 1557 ---	1-7, 26-90, 161-168
X	WO 01 17982 A (PIANETTI PASCAL MAURICE CHARLE ;GLAXO GROUP LTD (GB); FREEMAN GEOR) 15 March 2001 (2001-03-15) page 30, line 21 -page 33, line 28; claims 1-37 ---	1-7,14, 20-90, 161-168

-/-

## INTERNATIONAL SEARCH REPORT

PCT/US 03/12926

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 786 455 A (SHIONOGI & CO) 30 July 1997 (1997-07-30)  claims 7,8; tables 5,6 -----	1-7, 20-90, 112-138, 140-147, 161-168

**INTERNATIONAL SEARCH REPORT****PCT/US 03/12926****Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: 169-224, 229-232 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  
**4-7, 13, 14, 91-138, 140-160, partly: 1-3, 20-90, 161-168**
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box 3.

Claims Nos.: 169-224, 229-232

In claim 169, "MBF" is not clear to the skilled person; see for instance WO-A-0114361: " Example 2: Preparation of Monobenzyl fluorescein (MBF)"

There is no category for a claim directed to an "improvement"; see claim 170 in connection with Guidelines Ch. III. 3.1.

Apart from the fact that the expression "improvement" as such is unclear, the claims 171-201 attempt to define the subject-matter in terms of that unclear result to be achieved which merely amounts to a statement of the underlying (unclear) problem. The technical features necessary for achieving this result should have been added.

Likewise, claims 211 - 220 attempt to define the subject-matter in terms of the result to be achieved which merely amounts to a statement of the underlying problem. The technical features necessary for achieving this result should have been added.

The meaning of "half-life" in claim 232 is not precise; see Guidelines Ch. IV. 4.5.

A claim should be understandable without reference to the description. Therefore, claims 169, 202-210, 221 - 224, and 229-231 cannot be accepted under Art. 6, PCT; Rule 6.2(a) and Guidelines Ch. III. 4.10.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 6, 91-111, 132, 134, 140-147, partly claims 1-3, 20-90, 161-168

Capravirine-like phosphonate NNRTI compounds

2. Claims: 4, 133, partly claims 1-3, 20-90, 161-168

Phosphonate compounds of formula Ia

3. Claims: 5, 112-131, 135-138, 148-160, partly claims 1-3, 20-90, 161-168

Phosphonate compounds of formula Ib

4. Claims: 7, partly claims 1-3, 20-90, 161-168

Phosphonate compounds of formula Id

5. Claims: 8, partly claims 1-3, 20-90, 161-168

PETT-like phosphonate NNRTI compounds

6. Claims: 9, partly claims 1-3, 20-90, 161-168

Pyrazole-like phosphonate NNRTI compounds

7. Claims: 10, partly claims 1-3, 20-90, 161-168

Urea-PETT-like phosphonate NNRTI compounds

8. Claims: 11, partly claims 1-3, 20-90, 161-168

Nevapirine-like phosphonate NNRTI compounds

9. Claims: 12, partly claims 1-3, 20-90, 161-168

Quinazoline-like phosphonate NNRTI compounds

10. Claims: 13, partly claims 1-3, 20-90, 161-168

Evavirenz-like phosphonate NNRTI compounds

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

11. Claims: 14, partly claims 1-3, 20-90, 161-168  
Benzophenone-like phosphonate NNRTI compounds
12. Claims: 15, partly claims 1-3, 20-90, 161-168  
Pyrimidine-like phosphonate NNRTI compounds
13. Claims: partly 1-3, 16, 20-90, 161-168  
SJ-3366-like phosphonate NNRTI compounds
14. Claims: 17, partly claims 1-3, 20-90, 161-168  
Delavirdine-like phosphonate NNRTI compounds
15. Claims: partly 1-3, 16, 20-90, 161-168  
Emivirine-like phosphonate NNRTI compounds
16. Claims: 19, partly claims 1-3, 20-90, 161-168  
Loviride-like phosphonate NNRTI compounds
17. Claims: 18, partly claims 1-3, 20-90, 161-168  
UC781-like phosphonate NNRTI compounds
18. Claims: 140-147  
N-A2- imidazole derivatives
19. Claims: 148-160  
N-A1- imidazole derivatives
20. Claims: partly claims 1, 161-168  
NNRTI compounds containing phosphonate group(s) not comprised by inventions I-XIX
21. Claims: 225-228, 233-236

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Method of targeting a compound to white blood cells; the compound being not necessarily a NNRTI and the preparation of such compound

## INTERNATIONAL SEARCH REPORT

PCT/US 03/12926

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 0196329	A	20-12-2001		AP 200302716 D0 AU 6273301 A BR 0111678 A CA 2410763 A1 CN 1446213 T CZ 20023940 A3 EP 1295879 A1 WO 0196329 A1 NO 20026013 A	31-03-2003 24-12-2001 03-06-2003 28-11-2002 01-10-2003 14-05-2003 26-03-2003 20-12-2001 13-02-2003
WO 0203997	A	17-01-2002		AU 7367001 A CA 2405798 A1 CN 1440292 T CZ 20024052 A3 EP 1303282 A1 HU 0301614 A2 NO 20030033 A SK 112003 A3 WO 0203997 A1	21-01-2002 17-01-2002 03-09-2003 12-03-2003 23-04-2003 29-09-2003 03-01-2003 01-04-2003 17-01-2002
US 6312662	B1	06-11-2001		US 2002052345 A1 AU 3069999 A CA 2322487 A1 EP 1060182 A2 JP 2002505333 T WO 9945016 A2	02-05-2002 20-09-1999 10-09-1999 20-12-2000 19-02-2002 10-09-1999
US 5413996	A	09-05-1995		US 5177064 A US 5618803 A AT 150759 T AU 649466 B2 AU 8300091 A CA 2087194 A1 DE 69125377 D1 EP 0539493 A1 JP 5509313 T WO 9200988 A1	05-01-1993 08-04-1997 15-04-1997 26-05-1994 04-02-1992 14-01-1992 30-04-1997 05-05-1993 22-12-1993 23-01-1992
WO 0117982	A	15-03-2001		AU 7774300 A BR 0013771 A CA 2383782 A1 CN 1391565 T CZ 20020807 A3 WO 0117982 A1 EP 1208091 A1 HU 0202593 A2 JP 2003510252 T NO 20021042 A TR 200201187 T2	10-04-2001 14-05-2002 15-03-2001 15-01-2003 17-07-2002 15-03-2001 29-05-2002 28-12-2002 18-03-2003 30-04-2002 21-08-2002
EP 0786455	A	30-07-1997		AU 706095 B2 AU 4788896 A BR 9509024 A EP 0786455 A1 FI 971234 A JP 3155009 B2 NO 971306 A PL 320009 A1	10-06-1999 19-04-1996 30-09-1997 30-07-1997 23-05-1997 09-04-2001 21-05-1997 01-09-1997

**INTERNATIONAL SEARCH REPORT****PCT/US 03/12926**

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP 0786455	A	US	5910506 A	08-06-1999
		CA	2200316 A1	04-04-1996
		CN	1158609 A ,B	03-09-1997
		HU	77357 A2	30-03-1998
		WO	9610019 A1	04-04-1996
		RU	2157368 C2	10-10-2000
		TW	401404 B	11-08-2000
		US	6147097 A	14-11-2000